## REMARKS

Revocation and New Power of Attorney & Change of Correspondence Address

Applicants include a Power of Attorney and Correspondence Indication Form and a Statement under 37 C.F.R. §3.73(b) both signed by Janet Campbell, as CEO of the Assignee, SENO Medical Instruments, Inc. and appoints the undersigned to prosecute the above-referenced patent application before the U.S. Patent and Trademark Office.

Status of the claims

Claims 1-56 are pending and rejected herein. Claims 1, 13, 28, 30, 34--39, 47, and 54-56 are amended. Claims 2-4, 17, and 33 are canceled. New claims 57-60 are added. No new matter is added in any claim amendment.

Objections to the claims

Claim 55 is objected to because it is dependent on non-existing claim 59. Applicants have amended claim 55 to depend from claim 54. Accordingly, in view of these claim amendments, Applicants respectfully request that the objection to the claim numbering be withdrawn.

Amendments to the claims

The preamble of claim 1 is amended to recite "specific object or distribution thereof (pg. 4, ll. 16-18; pg. 58, ll. 19-22). Optically detecting a specific object in a body using the nanoparticulate contrast agents would show inherently how the detected object was distributed in the body. Also, claim 1 is amended to recite from "3" nm to 300 nm. Applicants submit this is a typographical error. The specification discloses that the wavelength must be at least 3 times that of the minimum characteristic dimension of the particle (Abstract) which is about 1 nm (pg. 4, ll. 18-20; pg. 5, ll. 23-27); therefore the minimum wavelength is 3 nm and not 300 nm. In addition, claim 1 also is amended to include all the limitations of dependent claim 2. Furthermore, claim 1 is amended to include a method step of "quantitatively characterizing said object(s) based on said assessment".

Claim 13 is amended to recite that the nanoparticles in the ordered aggregate are coated with "a targeting vector" (pg. 13, ll. 11-14) comprising organic material. New claim 57 is added which depends from claim 13 and limits the organic material to nucleosides, nucleotides, nucleotide acid constructs, polynucleotides, amino acids, peptides, oligopeptides, polypeptides, proteins, antibodies or antibody fragments thereof (pg. 13, ll. 14-20).

Claim 28 is amended to delete the phrase "block copolymers in which one block is" and to

limit the organic material to comprising the recited polyethylene glycol and to recite "a derivative thereof" (pg. 11, ll. 32 to pg. 12, ll. 5). Claim 30 is amended to delete the specific recited markers. Claim 34 is amended to depend from claim 32 as claim 33 is canceled and to delete the phrase "the particles comprise gold and". Claim 35 is amended to recite that the "nanoparticulates comprise mixed collections of gold and silver nanoparticles (pg. 10, ll. 11-14). Claim 36 is amended to recite that the "nanoparticles have a multimodal" distribution of aspect ratios (pg. 15, ll. 4-5). As such, claim 37 is amended to recite "another" local maximum because claim 36, from which claim 37 depends, now recites multimodal aspect ratios. Claim 38 is amended is recite "bands" instead of spreads to correspond to claim 39 which depends therefrom. Claim 39 is amended to recite "520" nanometers and "1120" nanometers to correspond to amended claim 34 from which claim 39 indirectly depends.

Claim 47 is amended to properly depend from claim 1. Claim 47 also is amended to recite "or distributions thereof", i.e., distributions of the tissue, cell, etc., to correspond to the same amendment in claim 1 and for the same reasons. New claim 59 is added which depends from claim 47 and limits the object to a bio-warfare agent (pg. 54, ll. 24 to pg. 55, ll. 33; Figs. 9A-9B)

Claim 54 is amended to recite "nanoparticulates" instead of particles as to correspond to the other claims. Claim 54 also is amended to clarify that the formed shape is non-spherical to correspond to the other claims and to correct grammar and method step identifiers. In addition claim 54 is amended to recite that the selected wavelength or range of wavelengths is larger by a factor of "3" and not 5 to correspond to claim 1. Claim 55 is amended to properly depend from amended independent claim 54.

Claim 56 is amended in the preamble and body of the claim to recite "a specific object" or "object", thereby corresponding to amended independent claim 1 and, with the exception of the next amendement, deletes "tumor". Claim 56 also is amended to recite that the object includes "a tumor or abnormal cells" (pg. 24, ll. 20-22; pg. 37, ll. 11-12; pg. 38, ll. 7, pg. 36, ll. 2-4). In addition claim 56 is amended to recite "non-spherical nanoparticulates" or "nanoparticulates" and the selected wavelength is larger by a factor of "3", as with claim 54.

New claim 58 depends from claim 14 and limits the form of carbon having metallic properties to a carbon nanotube (pg. 19, ll. 7-12; pg. 53, ll. 22 to pg. 54, ll. 4; Figs. 8A-8B).

New independent claim 60 is drawn to an optoacoustic imaging system for enhanced detection of a specific object in a body comprising the nanoparticulates of claim 1 and adapted to perform the method steps of claim 1. The optoacoustic imaging system also comprises a source of electromagnetic radiation (pg. 14, ll. 12-19), at least one acoustic transducer (pg. 57, ll. 3-8, 26-28; Figs. 9A, 11A), means for electronically amplifying and displaying the signals (pg. 57, ll. 5-8; Figs. 9A, 11A) as one- (Fig. 7A), two- (Figs. 7B, 8B) or three-dimensional images (Fig. 12A).

Additional claim fees

A total of 56 claims, including 4 independent claims, were filed with the instant application. Applicants have canceled 5 claims, including one independent claim, and added 4 new claims, including one independent claim. Thus, no additional claim fees are due. However, should Applicants err, please debit any additional claim fees from Deposit Account No. 07-1185, upon which the undersigned is allowed to draw.

Allowable subject matter

The Examiner states that claims 22 and 23 would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Applicants submit that pending claims 1, 5-16, 18-32, and 34-60, as amended herein, are allowable and respectfully request that the Examiner consider the arguments presented *infra*.

Amendments to the specification

Applicants have amended the specification to replace "optoacoustical" with "optoacoustic" as it refers to optoacoustic imaging. This is a grammar/spelling error and the correction thereof does not comprise new matter. The specification discloses and defines "optoacoustic imaging" (pg. 1, ll. 11-25; pg. 2, ll. 1-4).

The specification also is amended to disclose that the electromagnetic radiation has a specific wavelength or spectrum of wavelengths in the range from "3" nm to 300 mm, as discussed *supra* for the same amendments to claims 1 and 3. Applicants submit that this amendment does not constitute new matter.

The 35 U.S.C. §103 rejections

Claims 1-9 and 54-56 are rejected under 35 U.S.C. §103(a) as being unpatentable over **Henrichs** *et al.* (U.S. Patent No. 6,662,040) in view of **Link** *et al.* (International Reviews in Physical Chemistry, Vol. 19, No. 3, pp. 409-453). Applicants respectfully traverse this rejection.

In considering independent claims 1, 54 and 56, the Examiner states that **Henrichs** *et al.* teach a method of enhancing detection for a specific object in a body comprising a) administering to the body a nanoparticulate (col. 19, ll. 55-64) which is at least partially metallic (col. 25, ll. 45) and which inherently has a formed composition capable of producing thermal pressure either in the nanoparticulate or in the object greater than the object could produce as a result of EM radiation in the absence thereof and b) directing onto the body specific EM radiation (col. 2, ll. 3-9) having a wavelength or spectrum of wavelengths in the range from 300 nm to 300 mm (col. 8, ll. 40-64), e.g., visible and near infrared (col. 4, ll. 19-30) where the nanoparticulate absorbs the EM radiation (Abstract) and produces an enhanced optoacoustic signal resulting

from the absorption (col. 1, ll. 9-11). The Examiner states that that **Henrichs** *et al.* do not teach using a nanoparticles formed in a non-spherical shape having a minimal characteristic dimension from about 1 to about 3000 nm, but that **Link** *et al.* teach a method of detection enhancement using optical absorprtion porperties of metal nanoparticles having a non-spherical shape (Fig. 1) and a mean aspect ratio of 3.3 (pg. 413).

The Examiner concludes that it would be obvious to one of ordinary skill in the art to modify the apparatus and method of **Henrichs** *et al.* and to incorporate gold nanorods of **Link** *et al.* since the longitudinal plasmon resonance absorbing at longer wavelength is more effective in amplifying the fluorescence intensity in gold nanoparticles than the surface plasmon resonance of spheres possibly because **Link** *et al.* disclose that longitudinal plasmon resonance is less damped and has a much larger oscillator strength (pg. 423).

**Henrichs** *et al.* disclose an optoacoustic imaging method using a physiologically tolerable contrast agent having a radiation absorbing component and/or a pressure inducing component (Abstract). The contrast agent may be an organic dye compound that absorbs wavelengths of 300 to 1300 nm (col. 5, ll. 8-16), a heavy metal-containing compound, e.g., barium sulfate, that absorbs x-rays (col. 6, ll. 35-37) or superparamagnetic particles of a ceramic material, e.g., oxides of cobalt, manganese, nickel, or copper, that absorb microwaves (col. 6, ll. 62-67). The contrast agents may be solid particles, such as coated or uncoated crystalline structures, fluid particles, such as liquid particles in an emulsion or aggregates, i.e., fluid-containing liposomes (col. 7, ll. 1-16). The contrast agents may comprise targeting ligands, be coated with surfactants (col. 8, ll. 65-67)

**Link** *et al.* is an overview of the shape and size dependence of various radiative, non-radiative and photothermal properties of metallic nanocrystals (Abstract), such as surface plasmon resonance (pg. 415, Fig. 2 legend; pg. 420, Fig. 3 legend) and photothermal transformation (pg. 440, Fig. 13 legend). The properties of gold nanorods and spherical gold nanoparticles are examined (pg. 413, Fig. 1 legend). The fluorescence maxima red shifts in gold nanorods in a size dependent manner, but not in spherical gold nanoparticles, indicating that the longitudinal plasmon resonance absorbing at longer wavelengths is more effective in amplifying the fluorescence intensity in gold nanorods than in spherical gold nanoparticles (pg. 15, ll. 13-23). Femtosecond laser pulses cause photothermal transformation, i.e., change away from nanorod shape or melting, in gold nanorods (pg. 440, Fig. 13 legend).

Applicants have canceled claims 2-4 and added new claim 59. Applicants' invention, as recited in amended independent claims 1, 54, 56, and new claim 60 are drawn to methods of enhancing detection of a specific object in a body by using optoacoustic imaging methods and systems that employ the at least partially non-spherical nanoparticulates as recited in the claims. The wavelength used to radiate the nanoparticulates and the object is at least 3 times that of the minimal characteristic diameter of a collection of

the nanoparticulates The nanoparticulates absorb the electromagnetic radiation more than would one or more non-aggregated spherically shaped particles of the same total volume and composition identical to said nanoparticulate. This results in enhanced detection. In addition, amended claim 56 includes the step of treating the detected object by directing a wavelength that is minimally absorbed by the body so that only the nanoparticulates are heated to produce a sufficiently enhanced optoacoustic effect to destroy viability of the object.

A determination of obviousness requires a teaching or suggestion of all the claim elements in the combination of cited prior art which provides motivation for one of ordinary skill in the art to make the combination with a reasonable expectation of success not found in Applicants' specification. **Henrichs** *et al.* do not teach or suggest metal or partially metal nanoparticulates or nanoparticles. Nor do **Henrichs** *et al.* teach or suggest the formed nonspherical, at least partially metallic nanoparticulates recited in claims 1, 54, 56, and new claim 60. The Examiner stated that the particles in **Henrichs** *et al.* inherently have a formed composition capable of producing thermal pressure either in the nanoparticulate or in the object. First, for Applicants' nanoparticulates, an at least partially metallic nanoparticulate refers to a solid nanoparticulate composed of a single metal or to a metal shell filled with another substance (pg. 22, ll. 3-4). Thus, at least the outer surface or shell of the nanoparticulate is metal. **Henrichs** *et al.* do not teach these at least partially metallic nanoparticulates, but rather disclose that solid particles may be composed of an organic dye, may comprise a dye shell, may be a ceramic or metal oxide or a heavy metal compound, e.g., barium sulfate, as discussed *supra*. These are not Applicants non-spherical, at least partially metallic nanoparticulates.

Second, the instant invention defines "formed shape", in characterizing the nanoparticulates, as a shape that is fabricated or manipulated to increase one dimension more than the others in three dimensional space (pg. 6, ll. 3-5). This is an engineered physical feature designed to maximally shift the absorption maxima significantly toward longer wavelengths compared to spherical nanoparticles of the same total volume, composition and otherwise identical to the non-spherical nanoparticulates. In addition the instant nanoparticulates having the formed shape absorb electromagnetic radiation stronger than the corresponding spherical nanoparticulates (pg. 22, ll. 21-28). **Henrichs** *et al.* teach that solid particles are formulated as particles with diameter sizes between 5 and 10000 nm (col. 8, ll. 49-52). With no further guidance provided in **Henrichs** *et al.*, the implication is that all the diameters in a formulated particle are the same, such as in a spherical shape. Applicants reiterate that this is not Applicants' non-spherical, at least partially metallic nanoparticulate.

Combining **Link** *et al.* with **Henrichs** *et al.* cannot remedy these deficiencies. In viewing the combination of **Henrichs** *et al.* and **Link** *et al.*, one of ordinary skill in the art would find no motivation to use the gold nanorods disclosed in **Link** *et al.* in the methods of **Henrichs** *et al.* First, the combination neither teaches nor suggests that nonspherical, at least partially metallic nanoparticulates are useful in

photoacoustic imaging. **Henrichs** *et al.* do not teach or suggest at least partially metal nanoparticulates, as discussed supra. It would be apparent to one of ordinary skill in the art that **Link** *et al.* suggest that non-spherical gold nanoparticles would be less suitable as contrast agents for optoacoustic imaging than spherical gold particles. As pointed out by the Examiner, non-spherical gold nanoparticles (gold nanorods) fluoresce much more strongly than do spherical gold nanoparticles. However, enhanced fluorescence is disadvantageous for the enhancement of the optoacoustic response. The efficient generation of an optoacoustic signal depends on the conversion of the absorbed electromagnetic energy into heat, not back into light, i.e., luminescence or fluorescence. Particularly, **Henrichs** *et al.* teach that 1) efficient production of heat necessary for a photoacoustic effect requires minimal or weak concomitant fluorescence and phosphoresce and 2) the dye must only weakly fluoresce or phosphoresce at preferred wavelengths of 600-1300 nm because at these wavelengths absorbance by naturally occuring substances of the body is low. The fact that luminescence (fluorescence) of elongated nanoparticles increased from $10^{-10}$ to $10^{-5}$ compared to spherical nanoparticles, as taught by **Link** *et al.*, teaches away from using them for optoacoustic imaging. Thus, one of ordinary skill in the art has no motivation to make the combination.

Second, no reasonable expectation of succes is present for one of ordinary skill in the art in combining **Henrichs** *et al.* with **Link** *et al.* because **Henrichs** *et al.* teach that optoacoustic imaging requires minimal fluorescence from the dye and **Link** et al. teach that fluorescence in elongated nanoparticles increased so significantly. The teaching that elongated gold nanoparticles are highly efficient as optoacoustic contrast agents, in spite of the significantly increased fluorescence shown by **Link** et al., is only disclosed in Applicants' specification. Applicants demonstrate that elongated metal nanoparticles, particularly gold or silver nanoparticles, absorb electromagnetic energy very effectively and have an exceptionally strong value of optical absorption over organic dyes or spherical nanoparticles (Example I; pg. 50, ll. 1-21) and that effectively all of the optical absorption is converted to heat (Example II) all of which enhances optoacoustic contrast. The combination of **Henrichs** *et al.* and **Link** *et al.* neither teaches nor suggests these advantages.

Therefore, the combination of **Henrichs** *et al.* and **Link** *et al.* cannot render independent claims 1, 3, 54, and 56 nor new independent claim 60 obvious. Furthermore, claims 5-9 and 55 depend directly or indirectly from indpendent claims 1 and 54, respectively. If **Henrichs** *et al.* in combination with **Link** *et al.* cannot render independent claims 1, 3 and 54 obvious, then neither are dependent claims 2, 4-9 and 55 rendered obvious by the combination. Accordingly, in view of the claim amendments and arguments presented herein, Applicants respectfully request that the rejection of claims 1, 5-9 and 54-56 under 35 U.S.C. §103(a) be withdrawn.

Claims 10-53 are rejected under 35 U.S.C. §103(a) as being unpatentable over **Henrichs** *et al.* in view of **Link** *et al.* and in further view of **Oldenburg** *et al.* (U.S. Patent No. 6,344,272). Applicants

respectfully traverse this rejection.

The Examiner states that **Henrichs** *et al.* in view of **Link** *et al.* teach all the limitations of claim 6, but do not specifically teach that the nanoparticles are combinations of nanoparticles of one shape and nanoparticles of another shape made of various mixtures. The Examiner states that **Oldenburg** *et al.* teach a method of photoacoustic imaging using metal nanoshells comprising the use of particles that are mixtures, are homogeneous or non-homogeneous in size and are comprised of a nonconducting inner layer that is surrounded by an electrically conducting material (Abstract). The Examiner also states that **Oldenburg** *et al.* teach that the aggregate comprises spherical nanoparticles (Fig. 1) which may be partially coated with organic material, e.g., genetic material, or are gold, silver, platinum, a form of carbon having metallic properties, a mixture of at least two of the metals, or an alloy of at least two of the metals (col. 5, ll. 66 to col., 6, ll.9) and that the organic material is ambiphilic (col. 10, ll. 50-58). In addition the Examiner states that **Oldenburg** *et al.* teach that the nanoparticles have various probable sizes of diameters and are solid (col. 5, ll. 40-65) and that the absorbance maximums are insensitive to changes in particle size and nanoparticles have various dielectric coatings (col. 1, ll. 61-64). The Examiner further states that **Oldenburg** *et al.* teach that specially tailored particles or particle mixtures are added to vrious polymers, e.g., polyethelyne, PVA, etc., during preparation (col. 4, ll. 39-43) and/or contain carboxylic acid Linkages (col. 12, ll. 31-33). The Examiner concludes that it would be obvious to one of ordinary skill in the art to modify the apparatus and method of **Henrichs** *et al.* in view of **Link** *et al.* and to incorporate **Oldenburg** *et al.* to provide more efficient response following EM radiation and longer survival time of the nanoparticle.

**Oldenburg** *et al.* disclose particulate compositions, i.e., nanoshells, and methods of making the same (Abstract). The nanoshells have at least one non-conducting core layer (col. 5, ll. 35-40) and at least one conducting metal (col. 4, ll. 63 to col. 5, ll. 16; col. 6, ll. 5-9; ) or metal-like shell layer, i.e., and organic conducting material like polyacetylene or doped polyanaline (col. 6, ll. 1-3). The nanoshells are assembled by growing core particle, binding a linker molecule to the core and reacting the linker molecule with clusters of molecules comprising the conducting shell layer (col. 6, ll. 32-42).

Applicants have canceled claims 17, 33 and 35 and added new claims 57-59 as discussed *supra*. Applicants' invention is as discussed *supra* for amended independent claim 1. Claims 10-53 and new claims 57-59 depend directly from amended independent claim 1 or indirectly through dependent claim 6. As discussed *supra*, Applicants maintain that the combination of **Henrichs** *et al.* and **Link** *et al.* neither teaches or suggests using Applicants' at least partially metallic nanoparticulates for optoacoustic imaging as recited in amended independent claim 1 and, by extension, dependent claim 6. Combining **Oldenburg** *et al.* with **Henrichs** *et al.* and **Link** *et al.* still does not remedy this deficiency.

**Oldenburg** *et al.* neither teach nor suggest using the nanoshells for photoacoustic (optoacoustic) imaging. At best **Oldenburg** *et al.* disclose that particles or particle mixtures for selective

specially tailored for infrared absorption could be useful as mid-infrared detectors for medical imaging via photoconductive effects. Particularly, **Oldenburg** *et al.* disclose that solar cells or similar devices incorporating the specially tailored particles or mixtures and operated in a photoconductive instead of a photovoltaic mode could be used to provide new low-cost, compact infrared detectors for, *inter alia*, medical imaging (col. 4, ll. 52-62; col. 8, ll. 57-64). This is not optoacoustic imaging where an acoustic signal is detected. Also the instant nanoparticulates are used as contrast agents in an optoacoustic imaging system and not as infrared detectors.

Therefore, as the combination of **Henrichs** *et al.*, **Link** *et al.* and **Oldenburg** *et al.* cannot render amended independent claim 1 obvious, then neither are dependent claims 10-16, 18-32, 34, and 36-53 and new dependent claims 57-59 rendered obvious by the combination. Accordingly, in view of the claim amendments and arguments presented herein, Applicants respectfully request that the rejection of claims 10-16, 18-32, 34, and 36-53 under 35 U.S.C. §103(a) be withdrawn.

This is intended to be a complete response to the Office Action mailed September 10, 2007. Applicants submit that claims 1, 5-16, 18-32, and 34-60 are in condition for allowance and request that claims 1, 5-16, 18-32, and 34-60 be passed to issuance. If any issues remain outstanding, please telephone the undersigned attorney of record for immediate resolution. Applicants include a Petition for a One Month Extension of Time. Please charge the $60 petition fee to the credit card identified on the enclosed Form PTO-2038. **Only in the absence** of Form PTO-2038, please debit any applicable fees from Deposit Account No. 07-1185, upon which the undersigned is allowed to draw.

Respectfully submitted,

Date: Jan 9, 2008

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